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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,677	11/19/2003	Sean P. Palecek	960296.00101	9323

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EXAMINER

KIM, TAEYOON

ART UNIT	PAPER NUMBER
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1651

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09/27/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/717,677	PALECEK ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 August 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-13 and 16-28 is/are pending in the application.
- 4a) Of the above claim(s) 1,4-12,25 and 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13,16-24,26 and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>8/27/07, 8/13/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1, 4-13 and 16-28 are pending.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/13/07 has been entered.

Claims 2, 3, 14 and 15 are cancelled, claims 26-28 are newly added, and claims 1, 4-12, 25 and 28 are withdrawn from consideration as being drawn to non-elected subject matter. Claims 1, 16-24, 26 and 27 have been considered on the merits.

Claim Objections

Claims 16-24 and 27 are objected to because of the following informalities:

Claims 16-24 appear to be dependent on claim 13, which claims a cell culture composition. However, claims 16-24 are written as if they are drawn to "the culture" rather than "the cell culture composition". Applicant is advised to amend the claims to start with the term "The composition of Claim..."

Claim 27 is dependent on claim 26. However, claim 27 is drawn to "the method" of claim 26. It appears that claim 27 is supposed to be drawn to the composition rather than the method. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13, 16-24, 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell et al. (US 2002/0081726) in view of Xu et al. (2001) in light of Thompson et al. (1998).

Claims are drawn to a cell culture composition comprising human embryonic stem (hES) cells in culture without conditioned media or fibroblast feeder cells, a flexible solid porous matrix where the cells are grown, and an apparatus for applying periodic strain on the flexible matrix to stretch the matrix and cells thereon; a limitation to the cell being grown on Matrigel using BioFlex untreated culture plates; a limitation to the cells being grown without the presence of cross-species biological material; a limitation to the

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flexible solid porous matrix being Matrigel; a limitation to the strain being mechanically produced; a limitation to the flexible matrix being stretched using vacuum pressure; a limitation to the strain being from oscillatory stretching of the flexible matrix surface; a limitation to the strain exerted on the flexible matrix being at least about 5%; a limitation to the flexible matrix undergoing at least about 6 stretches per minute; a limitation to the stem cells being defined by the positive expression of Oct4 and SSEA-4 surface markers; a limitation to the undifferentiated human stem cells being alkaline phosphatase positive.

Russell et al. teach a hES cell culture composition (see paragraph [0106]) grown on hydrogel matrix (see paragraph [0015]), and an apparatus (Flexercell strain system (FX-3000) and BioFlex plate) (see paragraph [0161]) on which the cells are stretched by a vacuum (see paragraph [0146]). Russell et al. also teach the percentage of strain starting at 5% (see paragraph [0179]) and the frequency of strain or pattern of strain can be readily varied by programming the system (see paragraph [0146]).

Russell et al. do not teach the human embryonic stem cells being grown on Matrigel.

Xu et al. teach a culture of human embryonic stem (hES) cells on Matrigel without fibroblast feeder cells (see Abstract and Fig. 1). Xu et al. also teach undifferentiated hES cells on Matrigel in non-conditioned ES medium (see Fig. 1J). Xu et al. also teach the undifferentiated hES cells are positive for surface markers such as Oct4 and SSEA-4, and also positive for alkaline phosphatase (see Fig.1 and p.972, left column, 2nd paragraph).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to substitute the hydrogel taught by Russell et al. with Matrigel taught by Xu et al. because a person of ordinary skill in the art would recognize Matrigel would be an art-recognized equivalent matrix to the hydrogel for cell culture.

M.P.E.P. §2144.06 states "In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963) (Claims were drawn to a hollow fiberglass shaft for archery and a process for the production thereof where the shaft differed from the prior art in the use of a paper tube as the core of the shaft as compared with the light wood or hardened foamed resin core of the prior art. The Board found the claimed invention would have been obvious, reasoning that the prior art foam core is the functional and mechanical equivalent of the claimed paper core. The court reversed, holding that components which are functionally or mechanically equivalent are not necessarily obvious in view of one another, and in this case, the use of a light wood or hardened foam resin core does not fairly suggest the use of a paper core.); Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.)."

In regards to the limitations of "the hES cells proliferate and exhibit reduced

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differentiation relative to hES cells not subjected to periodic strain” or “differentiation is eliminated” in the claims, it is considered that the limitation does not provide any structural limitation to the claimed invention difference in comparison to the product disclosed by the references. Rather, the limitation merely states the result of the limitations in the claim and therefore, adds nothing to the patentability or substance of the claim. Therefore, this phrase does not limit the claim. See *Texas Instruments Inc. v. International Trade Commission*, 26 USPQ2d 1010 (Fed. Cir. 1993); *Griffin v. Bertina*, 62 USPQ2d 1431 (Fed. Cir. 2002); *Amazon.com Inc. v. Barnesandnoble.com Inc.*, 57 USPQ2d 1747 (Fed. Cir. 2001).

Claims 20-24 disclose method steps, and thus the claims are considered as product-by-process claims.

M.P.E.P. § 2113 reads, “Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps.”

“Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or

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where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)

The use of 35 U.S.C. §§ 102 and 103 rejections for product-by-process claims has been approved by the courts. "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Although the references above do not particularly teach the frequency of stretches or mode of stretching being oscillatory, it would have been obvious for a person of ordinary skill in the art because Russell et al. clearly indicates that varying patterns of strain (e.g. sinusoidal, stepwise, sustained, etc) can be readily programmed using factory-installed protocols using Flexercell strain unit (see paragraph [0146]), thus the various strain rate or the mode of stretching used in the claimed invention are result effective variables and effectively modified by programming the unit. As such, the

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variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of

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ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Response to Arguments

Applicant's arguments with respect to the previous office action based on Flexcell web page and Banes in view of Xu et al. and Thies have been considered, but are moot in view of the new ground(s) of rejection.

Applicant argued based on the IDS references filed on 8/13/07 and 8/27/07 asserting that the references teach that the mechanical stimulation is reported to induce differentiation in various cell types. Based on the teaching of these references, applicant asserted that it is not obvious that strain repress differentiation. The examiner respectfully disagrees with this assertion because whether or not the undifferentiated hES cells (as a starting culture) being stayed undifferentiated after culturing under the mechanical strain is clearly considered to be a result of method steps (i.e. culturing the hES cells), rather than the product claims. Thus, whether or not cells stayed undifferentiated does not make the current invention unobvious. Applicant is reminded that the current claims under examination are clearly drawn to the product rather than the method. Therefore, the references in combination (Russell et al. in view of Xu et al. in current office action) teaching undifferentiated hES cells, flexible porous matrix (Matrigel), without conditioned media or fibroblast feeder cells, and an apparatus capable of providing mechanical strain to stretch cells would render the claimed

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invention obvious.

It is noticed that in the argument against Xu et al. utilized as a secondary reference in the previous office action, applicant analyzes the teaching of Xu et al. individually, independent from the primary reference. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

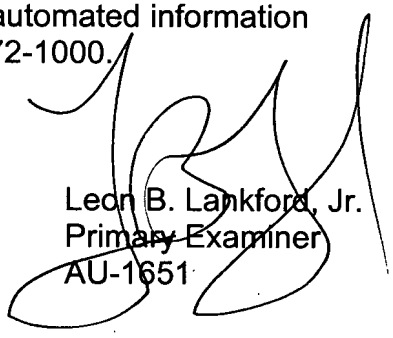
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 8:00 am - 4:30 pm ET (Mon-Fri).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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